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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ALLEN S. LAUGHON

Appeal 2008-005835
Application 09/810,385
Technology Center 1600

Decided: October 27, 2009

Before DONALD E. ADAMS, DEMETRA J. MILLS, and ERIC GRIMES, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134. The Examiner has rejected the claims for new matter and indefiniteness. We have jurisdiction under 35 U.S.C. § 6(b).

STATEMENT OF CASE

The following claim is representative.

9. A method for identifying compounds that directly interact with a Smad protein or a DNA-binding Smad corepressor protein to prevent protein-protein or protein-DNA interactions required for repression of transcription from genes induced by TGF-β, activin or bone morphogenetic protein signaling in cells comprising:

(a) detecting in a cell a first level of transcription of a reporter with a promoter which is regulated by a TGF-β, activin or bone morphogenetic protein signal, wherein said cell co-expresses interacting proteins comprising a Smad protein, a DNA-binding Smad co-repressor protein and a CtBP protein;

(b) contacting said cell with a test compound;

(c) detecting a second level of transcription of the reporter in the cell after addition of the test compound; and

(d) comparing the first level with the second level, wherein a decrease in the level of repression of transcription of the reporter in said cell after addition of the test compound is indicative of the ability of the test compound to interfere with transcriptional repression of genes induced by a TGF-β, activin or bone morphogenetic protein signal in cells.

Grounds of Rejection

1. Claims 9-12 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement for containing new matter.

2. Claims 9-12 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

New Matter Rejection

1. Claims 9-12 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement for containing new matter.

FINDINGS OF FACT

1. "The TGF-β superfamily is one of the largest groups of polypeptide growth and differentiation factors. A variety of structural and functional criteria have been used to group the superfamily into three classes: (1) TGF-β's; (2) activins; and (3) bone morphogenetic proteins (BMPs)." (Spec. 1.)
2. "TGF-β and its related factors, including activin, bone morphogenetic proteins (BMPs), and their *Drosophila* counterpart, decapentaplegic, each signal to their target cells by a unique signaling cascade activated by ligand-induced serine-threonine kinase receptor complex formation" (Spec. 2).
3. "TGF-β signaling pathways regulate transcription in cells by activating Smad proteins. Activated Smad complexes translocate to the nucleus where they activate target genes in coordination with interacting co-factors." (Spec. 7.)
4. "It is now well established that TGF-β signaling pathways switch target genes on through the activities of Smad proteins. These cytosolic proteins are recruited and phosphorylated by the TGF-β, activin, or BMP receptor complexes." (Spec. 2, emphasis added.)
5. "[A]lthough much is now known about how TGF-β pathways switch genes on, little is known about how gene can be switched off. There are examples of such negative regulation in vertebrates and in model organisms such as *C. elegans* and *Drosophila*." (Spec. 2.)

6. "Negative regulation by Smad proteins was also shown in *Drosophila*, where the *Drosophila* BMP4 [bone morphogenic protein] homolog, decapentaplegic (dpp), was shown to activate its targets by repressing expression of a novel repressor known as Brinker." (Spec. 2-3.)

7. "Ectopically expressed Brinker was able to repress BMP targets in frog embryos as well, indicating that this double negative mechanism is likely to operate in vertebrates as well as in *Drosophila*." (Spec. 3.)

8. "Using a Drosophila system, it has also been found that signaling by the TGF-β family member, Dpp, is negatively regulated by the brinker (brk) gene. . . . Like all TGF-β pathways, the Dpp pathway activates the Smad protein Mad, which forms a complex with its partner Smad, Medea, and regulates nuclear targets such as vg, Ubx, and tinman (tin). . . . The data now show that the brinker protein (Brk) binds and represses the Dpp response elements of vg and Ubx." (Spec. 10-11.)

9. The Specification states that "the present invention describes the interaction between Smad proteins and the general co-repressor dCtBP and shows how this interaction provides a mechanism for the ability of activated Smads to directly repress transcription in response to signaling" (Spec. 4).

10. The Specification states that

> [w]ith identification of the mechanism of . . . direct interaction of Smad proteins with co-repressors, assays can be developed, for example to identify proteins or small molecules tha interact with Smad proteins to prevent interaction of CtBP with Smads or with DNA-binding co-repressors . . . , or of formation of a DNA-bound complex containing Smads, CtBP and DNA-binding co-repressors, and thus prevent repression of genes that are negatively regulated by TGFβ signaling pathways.

(Spec. 14.)

11. The Specification, as filed, on page 4 states that:

> An object of the present invention is a method for identifying compounds that directly interact with Smad proteins, or with Smad co-repressors, to prevent protein-protein or protein-DNA interactions required for transcriptional repression in response to a TGFβ, activin, or bone morphogenetic protein signal which comprises determining changes in the level of transcription in cells, before and after addition of a test compound, wherein a decrease in the level of transcriptional repression is indicative of the ability of the test compound to interact with Smad proteins or Smad co-repressors to interfere with transcriptional repression that otherwise would occur in response to signaling by a TGFβ, activin or bone morphogenetic protein.

See also original claims 1 and 6.

12. The Declaration of Laughon states that the components, including promoters, used in the claimed assay were known at the time of filing of the '385 application and are those described in the '385 application. Laughon states:

> The components used in the assay were known at the time of filing of the '385 application and are those described in the '*385* application and depicted in Figure 6, namely Mad and Medea as Smad proteins, Shn [schnurri] as the DNA-binding Smad co-repressor protein, dCtBP, and lacz as the re-porter, the expression of which is controlled by the *brk* promoter, a direct target of Mad/Medea and schnurri (see abstract *of* Muller et al. (20031 *Cell* 113 :221-- 233; Exhibit A) .
>
> ... In this assay, repression of the *brk-lac2* reporter is caused by cotransfection of a plasmid that expresses TkvQD, an activated form of the type I Dpp receptor. Cotransfection with a plasmid expressing EIA blocks this repression by inhibiting CtBP. Accordingly, having used the well-known assay components and guidance provided in the specification for

> carrying out the method of the '385 application, we have successfully identified a compound that interferes with transcriptional repression of genes induced by a TGF-13 [sic, β], activin or bone morphogenetic protein signal in cells.

(Laughon Declaration, pages 1-2.)

13. The Examiner finds that,

> At most the passage contained within page 14, line 11 and page 15, line 12 mentions TGF-β- dependent reporter expression and one of ordinary skill in the art could assume that expression must be directed by a TGF-β promoter, but as noted in the FAOM mailed June 14, 2006 that may not happen under the exclusivity of the TGF-β promoter.

(Ans. 3-4.)

14. The Examiner finds that

> This section of the specification [page 14, line 11 to page 15, line 12] does not make mention of the activin or bone morphogenetic protein signal influencing transcription. Pages 9 and 10 of the specification do not exemplify the claimed method and pages 1-3 in no form or fashion seem to contemplate the claimed method implementing activin or a bone morphogenetic protein signal to regulate a promoter, which in turn directs transcription.

(*Id.* at 4.)

15. The Examiner finds that, "at best, one of ordinary skill in the art can assume there is a TGF-β promoter involved in the claimed method, clearly there is no support for activin or bone morphogenetic protein signal regulating a promoter." (*Id.*)

16. The Examiner finds that "none of the recited passages [in the Specification] list the reporter with a TGF-β-dependent promoter or activin

or bone morphogenetic protein signal within cells expressing specifically interacting proteins with the detection of transcription and the comparison between levels of transcription at precise points." (Ans. 4.)

PRINCIPLES OF LAW

When new matter is added to the claims, the proper course of action is to reject said claims for failing to satisfy the written description requirement of § 112, first paragraph. *In re Rasmussen*, 650 F.2d 1212, 1214 (CCPA 1981)("The proper basis for rejection of a claim amended to recite elements thought to be without support in the original disclosure, therefore, is § 112, first paragraph ..."). The purpose of the written description requirement is to "ensure that the scope of the right to exclude, as set forth in the claims, does not overreach the scope of the inventor's contribution to the field of art as described in the patent specification." *Reiffin v. Microsoft Corp.*, 214 F.3d 1342, 1345 (Fed. Cir. 2000). To that end, to satisfy the written description requirement, the inventor "must convey with reasonable clarity to those skilled in the art that, *as of the filing date sought*, he or she was in possession *of the invention*" [first emphasis added]. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). "One shows that one is 'in possession' of *the invention* by describing *the invention*, with all its claimed limitations" [emphasis in original]. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997).

We further point out that it is not necessary for the specification to describe the claimed invention *ipsis verbis*; all that is required is that it *reasonably* convey to those skilled in the art that, as of the filing date sought, the inventor was in possession of the claimed invention. *Union Oil Co. of*

California v. Atlantic Richfield Co., 208 F.3d 989, 997 (Fed. Cir. 2000); *Vas-Cath Inc. v. Mahurkar*, 935 F.2d at 1563-64; *In re Gosteli*, 872 F.2d 1008,1012 (Fed. Cir. 1989); *In re Edwards*, 568 F.2d 1349, 1351-52 (CCPA 1978). The test for determining compliance with the written description requirement is whether the disclosure of the application as originally filed reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter, rather than the presence or absence of literal support in the specification for the claim language. *See Vas-Cath, Inc. v. Mahurkar*, 935 F.2d at 1563-64 and *In re Kaslow*, 707 F.2d 1366, 1375 (Fed. Cir. 1983). Furthermore, claim language must be analyzed "not in a vacuum, *but always in light of the teachings of the prior art* and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art." *In re Moore*, 439 F.2d 1232, 1235 (CCPA 1971). [Emphasis added.]

ISSUE

The issue is: Has Appellant demonstrated error in the Examiner's new matter rejection or is there support in the application as filed for the claim 9 language "a promoter which is regulated by a TGF-β, activin or bone morphogenetic protein signal, wherein said cell co-expresses interacting proteins comprising a Smad protein, a DNA binding Smad co-repressor protein and a CtBP protein?"

ANALYSIS

The Examiner finds that

> This section of the specification [page 14, line 11 and page 15, line 12] does not make mention of the activin or bone morphogenetic protein signal influencing transcription. Pages 9 and 10 of the specification do not exemplify the claimed method and pages 1-3 in no form or fashion seem to contemplate the claimed method implementing activin or a bone morphogenetic protein signal to regulate a promoter, which in turn directs transcription.

(Ans. 4.) The Examiner finds that, "at best, one of ordinary skill in the art can assume there is a TGF-β promoter involved in the claimed method, clearly there is no support for activin or bone morphogenetic protein signal regulating a promoter." (*Id.*)

We do not agree with the Examiner's findings of fact and do not find, on the evidence before us, that the Examiner has established a prima facie case of new matter.

The Specification, as filed, on page 4 states that:

> An object of the present invention is a method for identifying compounds that directly interact with Smad proteins, or with Smad co-repressors, to prevent protein-protein or protein-DNA interactions required for transcriptional repression in response to a TGFβ, activin, or bone morphogenetic protein signal which comprises determining changes in the level of transcription in cells, before and after addition of a test compound, wherein a decrease in the level of transcriptional repression is indicative of the ability of the test compound to interact with Smad proteins or Smad co-repressors to interfere with transcriptional repression that otherwise would occur in response to signaling by a TGFβ, activin or bone morphogenetic protein.

See also original claims 1 and 6. (FF 11.) This passage of the Specification indicates that there is transcriptional repression in response to a TGF-β, activin, or bone morphogenetic protein signal. Thus, the original Specification supports transcriptional repression in response to a TGF-β, activin, or bone morphogenetic protein signal. In addition, the Specification states that Drosophila BMP4 (a bone morphogenic protein homolog), decapentaplegic (dpp), was shown to activate its targets by repressing expression of a novel repressor known as Brinker. (FF 6.) Dr. Laughon further clarifies that the promoter regulated by dpp, brk, is known in the art and described in the application.

> The components used in the assay were known at the time of filing of the '385 application and are those described in the '385 application and depicted in Figure 6, namely Mad and Medea as Smad proteins, Shn as the DNA-binding Smad co-repressor protein, dCtBP, and lacz as the re-porter, the expression of which is controlled by the *brk* promoter, a direct target of Mad/Medea and schnurri (see abstract *of* Muller et al. (20031 *Cell* 113 :221-- 233; Exhibit A).

(Laughon Declaration, 2, FF12.) Thus, the Specification as filed discloses a promoter which is regulated by a BMP, the brk promoter, which is a target of the BMP, Dpp.

Appellant further contends that

> Appellant exemplifies reporter constructs containing promoters *(e.g.,* the *wingless* promoter), which are regulated by such signals in cell based assays, wherein cells of the assays co-express interacting proteins comprising a Smad protein, a DNA-binding Smad co-repressor protein and a CtBP protein. See pages 9 and 10.

(App. Br. 7-8.) We agree with Appellant that the Specification's examples using proteins in the TGF-β superfamily that are not TGF-β itself, is evidence that the Specification's reference to "TGF-β signaling pathways" (e.g., on pages 14-15) generically encompasses signaling pathways of the TGF-β superfamily, including activin and bone morphogenetic proteins.

We find that Appellant has shown support in the original disclosure for promoters regulated by bone morphogenetic protein, and that such promoters are known in the art. *See* Laughon Declaration, FF12. We find that the Examiner has provided no evidence that persons of skill in the art would understand that the claimed promoter which is regulated by a TGF-β, activin or bone morphogenetic protein signal was not disclosed in the original specification. The new matter rejection is reversed.

CONCLUSION OF LAW

Appellant has demonstrated error in the Examiner's new matter rejection or is there support for the claim 9 language "a promoter which is regulated by a TGF-β, activin or bone morphogenetic protein signal." The new matter rejection is reversed.

Indefiniteness

2. Claims 9-12 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

ISSUE

The Examiner finds that claim 9, line 3 cites a "bone morphogenetic protein signal." The Examiner concludes that it is not clear what this signal

is and how it regulates a promoter. The Examiner thus finds that the metes and bounds cannot be determined. (Ans. 5.)

Appellant contends that one of ordinary skill in the art would clearly understand what is meant by a TGF-β, activin or bone morphogenetic protein signal. (App. Br. 8.)

Issue: Has the Examiner established that one of ordinary skill in the art would not have understood the phrase "bone morphogenetic protein signal?"

FINDINGS OF FACT

17. Claim 9 recites "a TGF-β, activin or bone morphogenetic protein signal" (Claim 9).

PRINCIPLES OF LAW

One of the purposes of 35 U.S.C. § 112, second paragraph,

> [I]s to provide those who would endeavor, in future enterprise, to approach the area circumscribed by the claims of a patent, with the adequate notice demanded by due process of law, so that they may more readily and accurately determine the boundaries of protection involved and evaluate the possibility of infringement and dominance.

In re Hammack, 427 F.2d 1378, 1382 (CCPA 1970) (citations omitted). As set forth in *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 1217 (Fed. Cir. 1991):

> The statute requires that "[t]he specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." A decision as to whether a claim is invalid under this provision requires a determination whether those skilled in the art would understand what is claimed. *See*

> *Shatterproof Glass Corp. v. Libbey-Owens Ford Co.*, 758 F.2d 613, 624, 225 USPQ 634, 641 (Fed. Cir. 1985) (Claims must "reasonably apprise those skilled in the art" as to their scope and be "as precise as the subject matter permits.").

Furthermore, claim language must be analyzed "not in a vacuum, but always in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art." *In re Moore*, 439 F.2d 1232, 1235 (CCPA 1971).

"[A]mbiguity in claim scope is at the heart of the definiteness requirement of 35 U.S.C. § 112, ¶ 2." *Amgen Inc. v. Hoechst Marion Roussel, Inc.*, 314 F.3d 1313, 1342 (Fed. Cir. 2003).

ANALYSIS

The Examiner finds that claim 9, line 3, cites a "bone morphogenetic protein signal." The Examiner finds that it is not clear what this signal is and how it regulates a promoter. The Examiner thus finds that the metes and bounds cannot be determined. (Ans. 5.)

The Specification, as filed, on page 4 states that:

> An object of the present invention is a method for identifying compounds that directly interact with Smad proteins, or with Smad co-repressors, to prevent protein-protein or protein-DNA interactions required for transcriptional repression in response to a TGFβ, activin, or bone morphogenetic protein signal which comprises determining changes in the level of transcription in cells, before and after addition of a test compound, wherein a decrease in the level of transcriptional repression is indicative of the ability of the test compound to interact with Smad proteins or Smad co-repressors to interfere with transcriptional repression that

> otherwise would occur in response to signaling by a TGFβ, activin or bone morphogenetic protein.

See also original claims 1 and 6. (FF7.) Thus the Specification indicates that a decrease in the level of transcriptional repression is indicative of the ability of the test compound to interact with Smad proteins or Smad co-repressors to interfere with transcriptional repression that otherwise would occur in response to signaling by a TGFβ, activin or bone morphogenetic protein, in other words a TGFβ signal, an activin signal or bone morphogenetic protein signal.

We do not find that the Examiner has established a prima facie case of claim indefiniteness. The Examiner has provided no evidence why one of ordinary skill in the art would not have understood this phrase.

CONCLUSION OF LAW

The Examiner has not established that one of ordinary skill in the art would not have understood the phrase "bone morphogenetic protein signal."

REVERSED

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